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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/173,821 10/16/98 RUDLAND P 32040PCTUSA-

HM12/0523

BAKER & BOTTS  
30 ROCKEFELLER PLAZA  
NEW YORK NY 10112-0228

EXAMINER

KAUSHAL, S

ART UNIT	PAPER NUMBER
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1633

18

DATE MAILED:

05/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/173,821	RUDLAND ET AL.
	Examiner	Art Unit
	Sumesh Kaushal	1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 09 March 2001.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1,4,6-9,13 and 15-32 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1,4,6-9,13 and 15-32 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

15) Notice of References Cited (PTO-892) 18) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.

16) Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) Notice of Informal Patent Application (PTO-152)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_. 20) Other: \_\_\_\_\_.

## DETAILED ACTION

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/09/01 has been entered.

Applicant's response filed on 03/09/01 have been fully considered but is found unpersuasive for the reasons of record as set forth in the earlier office action (Paper No.13, 12/15/00. Claim 3 is canceled. Claims 1, 4, 6-7 and 19-20 are amended. Newly filed claims 30-32 are entered. Claims 1, 4, 6-9, 13 and 15-32 are pending in this application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 112***

Claims 1, 4, 13, 15-17, 19-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for i) a neuronal cell line obtained from a transgenic rat comprising NF2 rat brain cells (NS-LtsA58) encoding human NF-L gene promoter and ii) a transgenic rat comprising B2LT1 rat mammary cells (MMTV-SV40tsA58) encoding human NF-L gene promoter, MMTVLTR-TGF $\alpha$  and MMTVLTR-C-erb-B-2, does not reasonably provide enablement for a neuronal cell line and/or a transgenic rat comprising any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope

with these claims, for the same reasons of record as set forth in the official action mailed on 12/15/00.

Applicant's response filed 03/09/01 (page 4) has been fully considered. Applicant argues that recitation of "cell line" to neuronal cell line" obviate this rejection. However, this is found unpersuasive for the same reasons of record as set forth in the official action mailed on 12/15/00 because the scope of instant claims encompass a neuronal cell line or transgenic rat comprising any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters. However, the instant specification is only enabled for i) cell line derived from transgenic rat comprising: B2LT1 rat mammary cells (MMTV-SV40tsA58) and NF2 rat brain cells (NS-LtsA58) ii) transgenic rats comprising: MMTVLTR-TGF $\alpha$  and MMTVLTR-C-erb-B-2. It is important to note that, the scope of the claims include rats encoding any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters. As stated in earlier official action (page 2, para.2), the transgene expression and physiological consequences of transgene products are not always accurately predictable because cis elements are controlled differently by various transacting factors in the genome of an animal. Therefore, the skilled artisan at the time of filing would be lacking a reasonable expectation of success for making neuronal transgenic cell lines derived from transgenic rat(s), comprising any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters, without having to engage in an undue amount of experimentation for the breadth of the claims.

*Claim Rejections - 35 USC § 103*

Claims 1, 4, 6-9, 13, 15-32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Noble et al (WO 91/13150, 1991), Stocklin et al (J. Cell Bio. 122(1):199-208, 1993), and Moses JH (Br. J. Cancer. 69(21):1, 1994) in view of Reeben et al (Biochem. Biophys. Res. Com. 192(2):465-470, 1993) in view of Leder et al (US Pat No. 5087571, 1992) and further in view of

Hammer et al (US Pat. No. 5489742, 1996). The references cited herein are of record in the official action(s) mailed on 8/17/99 and 5/15/00.

The applicant argues that the claimed invention is not rendered obvious by the cited art. The applicant has amended the claim to read upon a “neuronal cell line”. The applicant further argues that one ordinary skill in the art with the motivation to combine the references would not have a reasonable expectation of success. The applicant further argues that it is an unexpected result that human NF-L promoter when introduced into transgenic rats, as opposed to mice, would result in a completely unique tissue specific expression in the brain of transgenic rats.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Noble et al teaches transgenic animals and cell lines from any cell type of the animal body, wherein the cell line comprises SV40tsA58 immortalizing gene (fig-1; page 34, line 1-20, page 35-40, page 50, line 19, page 53, line 22, page 56, line 16, page 59, example-3, page 61 example-4 page 64, example-5 page 69, example-6, page 74, example-7). Noble also clearly teaches the making of cell lines derived from the central nervous system, for example the making of astrocytes and glial precursor cell lines (see page 53 line 22, page 61 example-4, page 64 example-5).

Stocklin et al teaches a transgenic mice wherein the human c-erbB-2 is operably linked to MMTV enhancer/promoter sequence wherein the transgene is expressed in kidney, lung, mammary, muscle, spleen, brain and liver cells (page 200, col.2 para.5, page 201, fig-1, col.2 para 2-3, page 202, table-II). Moses teaches a transgenic mice expressing a gene encoding human TGF- $\alpha$  under the control of MMTV enhancer/promoter (page 1, s1).

However, Noble et al, Stocklin et al and Mosses does not teach the use of human neurofilament (NF-L) promoter to derive the expression of SV40tsA58, c-erbB-2 and TGF-a genes. Yazdanbakhsh et al teaches human neurofilament (NF-L) promoter which regulates neuronal-specific expression (page 455, abstract). Yazdanbakhsh et al clearly teaches that the highest level of transgene expression occurs in the brain, including that the regulatory sequences that direct tissue-specific expression are present on hu NF-L fragment used (see page 459, col.1 line 8, fig-4).

Leder et al teaches method of providing a cell line from a transgenic mice encoding a transforming oncogene operably linked to mammary specific promoter MMTVLTR (col.4 line 13-22, col.9 line 11-20). Leder et al also teaches the use of transgenic mice for testing a material suspected of being a carcinogen (col.8 line 50-68). The cited art also teaches a method of testing a material for its ability to confer protection against the development of neoplasms using transgenic animals (col.9 line 1-9).

Although the combination of Noble et al, Stocklin et al, Mosses, Yazdanbakhsh et al Leder et al teaches a transgenic mice and/or cell line and a method of screening carcinogens, wherein in the transgenic cell the human neurofilament (NF-L) promoter to derive the expression of SV40tsA58, c-erbB-2 and TGF-a genes, it does not teach the making of a transgenic rat by super ovulating a female rat by continuous supply of FSH hormone..

Hammer et al teaches a method for producing transgenic rats, by super ovulating a female rat by continuous supply of FSH hormone using a mini-pump and introduction of the selected transgene into the fertilized eggs (col.15 line 60-67, col.1, line 1-17).

Thus, it would have been obvious to one ordinary skill in the art at the time of filing to have substituted the transgenic mice (encoding human neurofilament promoter which derives the expression of SV40tsA58, c-erbB-2 or TGF-a gene) as taught by Noble et al, Stocklin et al, Mosses and Yazdanbakhsh et al with a transgenic rat as taught by Hammer et al. It would have

been further obvious to test a material suspected of being carcinogen a transgenic rat as taught by Leder. One would have been motivated to do this because rats are widely used in biomedical research, and in addition to transgenic mice, a transgenic rat model would provide a two fold experimental approach for the same transgene.

In addition, the expression of hu NF-L regulated gene expression in the brain of rat is not an unexpected result because Yazdanbakhsh et al clearly teaches that the highest level of transgene expression occurs in the brain, including that the regulatory sequences that direct tissue-specific expression are present on hu NF-L fragment used (see page 459, col.1 line 8, fig-4). Thus, the invention as calimed is *prima facie* obvious in view of cited refereces.

### *Conclusion*

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Deborah Clark can be reached on (703) 305-4051. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Tracey Johnson, whose telephone number is (703) 308-0377. If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (<http://www.uspto.gov>) and **A CLEAN COPY OF ALL PENDING CLAIMS IS REQUESTED** to facilitate further examination.

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